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Nickel-catalyzed deallylation of aryl allyl ethers with hydrosilanes

Jingyang Wang^{a,1}, Yu Wang^{a,1}, Guangni Ding^b, Xiaoyu Wu^a, Liqun Yang^a, Sijie Fan^c, Zhaoguo Zhang^{a,d}, Xiaomin Xie^{a,*}^a Shanghai Key Laboratory for Molecular Engineering of Chiral Drugs, School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, China^b School of Materials Science and Engineering, Nanchang University, Nanchang 330031, China^c School of Chemistry and Chemical Engineering, Guangxi University, Nanning 530004, Guangxi, China^d Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Fenglin Road, Shanghai 200032, China

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ABSTRACT

An efficient and mild catalytic deallylation method of aryl allyl ethers is developed, with commercially available Ni(COD)₂ as catalyst precursor, simple substituted bipyridine as ligand and air-stable hydrosilanes. The process is compatible with a variety of functional groups and the desired phenol products can be obtained with excellent yields and selectivity. Besides, by detection or isolation of key intermediates, mechanism studies confirm that the deallylation undergoes η^3 -allylnickel intermediate pathway.

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Introduction

Selective protection or deprotection of functional groups is an important subject in organic synthesis [1]. As one of the most extensively used protecting groups in organic chemistry [2], especially for the protection of alcohols and phenols, allyl groups are not only easily available and stable towards both acidic and basic conditions, but also the deprotection may occur efficiently and selectively under mild conditions [3,4]. Traditional deallylation methods generally involve olefin isomerization process driven by strong bases and then breakage of enol ethers [5–10]. Moreover, oxidative systems [11,12], free radical processes [13,14], iodine-promoted processes [15–17], Lewis acid-promoted methods [18–20] and electrochemical strategies [21–23] have also been reported for deallylation. In recent years, due to the development of transition metal catalysis reactions, transition metal-catalyzed methods provide a promising alternative to the traditional deallylation tactics, because of high efficiency, good compatibility and mild reaction conditions [2,29]. Many transition metal-catalyzed deallylation methods have been reported, such as Ti [24,25], Rh [26,27], Pd [28–34], Ru [35–37], Fe [38], and Co [39] catalyzed

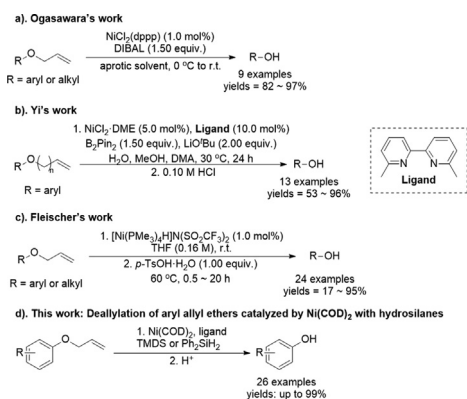
deallylation. However, most of these methods require for the use of noble metals as the catalysts.

Nickel catalyst is one kind of significant and extensively-used earth-abundant metal catalysts [40,41]. On account of its similar catalytic activity and stronger affinity to oxygen atom than conventional palladium catalysts, nickel-catalyzed deallylation is attractive [42]. Ogasawara's group developed a NiCl₂(dppp) (1,3-bis(diphenylphosphanyl)propane) catalyzed deallylation system of allyl ethers in the presence of stoichiometric amount DIBAL (diisobutylaluminum hydride) (Scheme 1a) [43]. With NiCl₂-DME (1,2-dimethoxyethane) as the catalyst and an excess amount of B₂Pin₂ and LiO^tBu, Yi's group realized the removal of various alkene protecting groups for phenols (Scheme 1b) [44]. Fleischer's group reported [Ni(PMe₃)₄H]NTf₂ catalyzed deallylation of allyl ethers via olefin isomerization and the following hydrolysis with *p*-TsOH·H₂O (Scheme 1c) [45]. With all the examples taken into consideration, there remains a need to develop a simpler, milder and more efficient protocol for nickel-catalyzed selective deallylation methodology.

Transition metal-catalyzed deallylation generally involves olefin isomerization process catalyzed by the metal-hydride species [28–30], or the cleavage of C–O bond of allyl ethers by oxidative addition in the presence of a nucleophile via η^3 -allylmetal intermediate [31–34]. Hydrosilanes are very appealing in organic synthesis, which are readily accessible, easy-to-handle and can

* Corresponding author.

E-mail address: xiaominxie@sjtu.edu.cn (X. Xie).¹ These authors contributed equally to this work



Scheme 1. Nickel-catalyzed deallylation methods.

be activated under mild conditions. In metal-catalyzed reactions, hydrosilanes may work as the hydrogen source of metal-hydride species or a nucleophile. Therefore, we explored the nickel-catalyzed deallylation in the presence of hydrosilanes. Herein, we report highly efficient and selective nickel/substituted bipyridine catalyzed deallylation of various aryl allyl ethers under mild conditions with easily available and air-stable hydrosilanes (Scheme 1d).

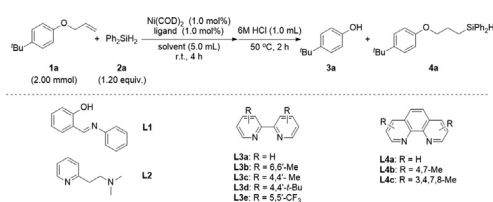
Results and discussion

We commenced our studies with the model reaction of 1-(allyloxy)-4-(*tert*-butyl)benzene (**1a**) and Ph₂SiH₂ (**2a**) in the presence of Ni(COD)₂ as the catalyst. We first tested some easily available phosphine and nitrogen ligands (Table 1, entries 1–7). For monodentate and bidentate phosphine ligands, the reactions had good

conversion, but tended to afford the hydrosilylation product **4a** as the main product (entries 1–2). When the nitrogen ligands were involved, the yield of the desired deallylation product **3a** increased. We were delighted to find that bidentate nitrogen ligands with bipyridine skeleton displayed relatively high reactivity and the best selectivity for the deallylation product **3a** (entry 6). Next, the effect of electronic nature and steric hindrance of the bipyridine ligands on the nickel-catalyzed deallylation was evaluated (entries 8–13). We found that using bipyridine with a bulky electron-donating *tert*-butyl group at the *para*-position as the ligand increased the yield of the deallylation product **3a** to 91% (entry 10). Ligands with electron-withdrawing substituents or substituents at the *ortho*-position demonstrated lower reactivity and would favor the formation of the hydrosilylation product **4a**. Therefore, 4,4'-di-*tert*-butyl-2,2'-bipyridine (**L3d**) was chosen as the optimal ligand. The effect of solvents on the deallylation was then examined. Besides THF, the deallylation could proceed smoothly in other solvents (entries 14–16). In polar solvent DMF, the desired deallylation product **3a** could be obtained in nearly quantitative yield with excellent selectivity (entry 16). However, nonpolar solvents like toluene or DCE, were not compatible for the deallylation (entries 17–18).

After that, we employed various commercially available hydrosilanes to test the effect of their structures and properties on the deallylation (Table S1). Most of the hydrosilanes, even the cheapest hydrosilane, PMHS (polymethylhydrosiloxane), could promote the deallylation with high efficiency and excellent selectivity. In consideration of reactivity, cost as well as easy work-up steps, we eventually chose Ph₂SiH₂ (**2a**) or TMSD (1,1,3,3-tetramethylidisiloxane, **2b**) in the deallylation. Moreover, using Ni(COD)₂ (DQ) (DQ : tetramethyl-*p*-benzoquinone), a relatively stable Ni(0) complex, as the catalyst, the decreased reactivity was observed (Table S1, entries 9 and 10). When Ni(OAc)₂ was used as the cata-

Table 1
 Optimization of reaction conditions.^a

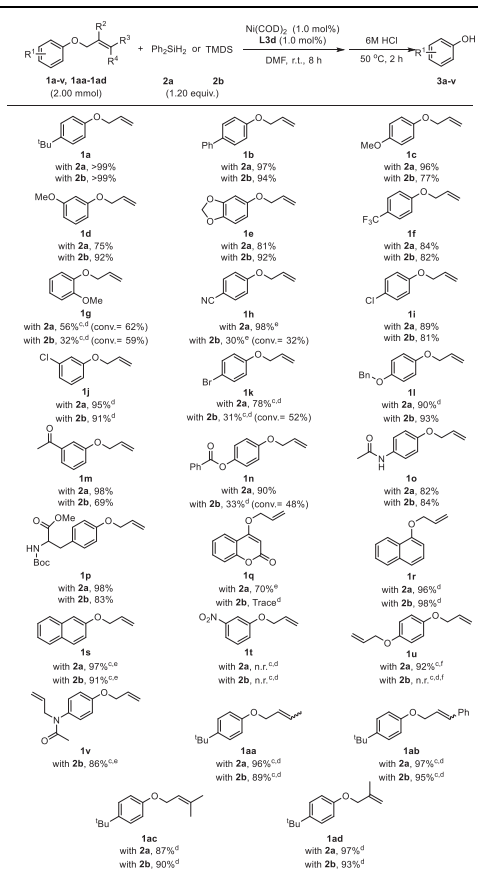


| entry | ligand | solvent | conv. ^b (%) | 3a ^b (%) | 4a ^b (%) |
|----------------|------------------|--------------------|------------------------|----------------------------|----------------------------|
| 1 ^c | PPh ₃ | THF | 94 | 2 | 54 |
| 2 | DPPE | THF | 95 | 5 | 67 |
| 3 | L1 | THF | 92 | 8 | 77 |
| 4 | TMEDA | THF | 69 | 7 | 56 |
| 5 | L2 | THF | 89 | 15 | 33 |
| 6 | L3a | THF | 98 | 88 | 8 |
| 7 | L4a | THF | 97 | 76 | 14 |
| 8 | L3b | THF | 56 | 20 | 34 |
| 9 | L3c | THF | >99 | 87 | 10 |
| 10 | L3d | THF | >99 | 91 | 8 |
| 11 | L3e | THF | 61 | 10 | 51 |
| 12 | L4b | THF | 97 | 2 | 80 |
| 13 | L4c | THF | 96 | 26 | 68 |
| 14 | L3d | 1,4-dioxane | 98 | 93 | 3 |
| 15 | L3d | CH ₃ CN | >99 | 94 | 3 |
| 16 | L3d | DMF | >99 | 98 | N.D. |
| 17 | L3d | toluene | 2 | Trace | N.D. |
| 18 | L3d | DCE | N.R. | N.D. | N.D. |

^a Reagents and conditions: **1a** (2.00 mmol), Ph₂SiH₂ (**2a**, 2.40 mmol), Ni(COD)₂ (1.0 mol%), ligand (1.0 mol%), solvent (5.0 mL) under a N₂ atmosphere, room temperature, 4 h. Then, 6 M HCl (1.0 mL), 50 °C, 2 h.

^b Conversions and yields were determined by GC analysis using 1,2,4,5-tetramethylbenzene as internal standard.

^c PPh₃ (2.0 mol%).

Table 2
Substrate scope.^{a,b}

^aReagents and conditions: aryl allyl ether (**1**, 2.00 mmol), **2a** or **2b** (2.40 mmol), Ni(COD)₂ (1.0 mol%), **L3d** (1.0 mol%), DMF (5.0 mL) under a N₂ atmosphere, room temperature, 8 h.

Then, 6 M HCl (1.0 mL), 50 °C, 2 h.

^bIsolated yields of corresponding phenol product **3**.

^cNi(COD)₂ (2.0 mol%) and **L3d** (2.0 mol%).

^d80 °C.

^e50 °C.

^f**2a** or **2b** (4.80 mmol).

lyst precursor, the deallylation also occurred smoothly with Ph₂SiH₂; while, the reduced reactivity with TMDS was obtained (Table S1, entries 11 and 12). However, replacement of Ni(COD)₂ with Ni(acac)₂ or NiCl₂(DME) had detrimental effect on the deallylation (Table S1, entries 13 and 14).

So far, the optimal reaction conditions were determined by using 1.0 mol% of Ni(COD)₂ as catalyst precursor, 1.0 mol% of 4,4'-di-*tert*-butyl-2,2'-bipyridine (**L3d**) as the ligand, and adding 1.20 equivalents of Ph₂SiH₂ (**2a**) or TMDS (**2b**), the deallylation could be conducted effectively and selectively in DMF at room temperature within 4 h.

The scope of aryl allyl ether substrates on deallylation was then investigated. As shown in Table 2, our simple and mild nickel-catalyzed deallylation demonstrated good to excellent reactivity and selectivity for various aryl allyl ethers. The catalytic system was not sensitive to electronic nature of aryl allyl ethers. A wide range of aryl allyl ethers **1**, possessing either electron-donating or electron-withdrawing substituents at varied positions, reacted smoothly to obtain their corresponding phenol products in excellent yields (Table 2, 1a-1f). Nevertheless, decreased yield was observed in the case of the aryl allyl ether with a methoxyl group on *ortho*- position (**1g**). Diverse valuable functional groups were well tolerated under this mild condition (**1h-1s**), furnishing a series

of phenol products in good to excellent yields. For halogenated substrates, no dehalogenated products were detected along with deallylation products (**1i-1k**). It's worth mentioning that the sensitive cyano (**1h**), ketonic carbonyl (**1m**), ester (**1n**), amide (**1o**) and lactone (**1q**) moieties were all compatible in the deallylation, with no reduction product observed. As for the selectivity of our deallylation system, when the substrate is modified with multiple protecting groups, including methyl group (**1c**), benzyl group (**1l**) and *tert*-butyloxy carbonyl group (**1p**), the deallylation could be carried out selectively, while the other protecting groups could be completely retained. For the substrate with two allyl ether moieties (**1u**), the bi-deallylated product, hydroquinone (**3u**), was obtained in excellent yield with increased loading of the catalyst Ni(COD)₂ and doubled equivalents of Ph₂SiH₂ (**2a**). In the case of the substrate modified with both the allyl ether moiety and the allyl amine moiety (**1v**), the selective *O*-deallylation product *N*-allyl-*N*-(4-hydroxyphenyl)acetamide (**3v**) could be obtained in 86% yield, with 12% of the *N*-(4-hydroxyphenyl)acetamide (**3v'**) formed. Moreover, we also tested some substrates with substituted allyl groups on either terminal or branched site (**1aa-1ad**), and all of them were effectively deallylated to give 4-(*tert*-butyl)phenol (**3a**) in excellent yields, with slightly elevated temperature. This indicates that the deallylation process is not affected by the steric hindrance on the allyl group side. In addition, when TMDS (**2b**) is used in the deallylation, some aryl allyl substrates could not be effectively deallylated (**1h**, **1k**, **1n** and **1q**), mainly due to the low reactivity. The substrate with the nitro group (**1t**) was not converted even under strong reaction conditions.

Then, gram-scale reactions were conducted to demonstrate the practicality of this method. Subjecting 1-(allyloxy)-4-(*tert*-butyl)benzene (**1a**) on a 15.00 mmol scale to both Ph₂SiH₂ (**2a**) and TMDS (**2b**) systems under mild reaction conditions delivered the desired deallylation product **3a** (2.00 g and 1.87 g) in 89% yield and 83% yield, respectively (Scheme 2).

We next turned our attention to mechanistic studies. As mentioned before, the transition-metal catalyzed deallylation may be initiated by metal hydride and *via* olefin isomerization. It is also possible that the deallylation begins with the oxidative addition between the low valence metal and the substrate to form the η³-allylmetal intermediate. To investigate the mechanism of our deallylation system, several control experiments were designed and conducted.

As shown in Table 3, both the metal catalyst and the hydrosilane are indispensable for the deallylation (Table 3, entries 2–3). In the absence of the ligand, the selectivity remarkably shifted to the hydrosilylation (entry 4). When a catalytic amount of hydrosilane was employed, most of the substrate was recovered (entry 5), and a complete conversion of **1a** required for a stoichiometric amount of hydrosilane (entry 6). These results indicated that the deallylation is not initiated by the nickel hydride formed from the reaction of Ni(COD)₂ and the hydrosilane, as a catalytic amount of the nickel hydride is capable of realizing effective olefin isomerization of the aryl allyl ether substrate. Furthermore, using **1a** and Ph₂SiH₂ (**2a**), we monitored the reaction progress before the hydrolysis process by GC-MS. Both the silyl aryl ether intermediate bis(4-(*tert*-butyl)phenoxy)diphenylsilane (Scheme 3, II) and the olefin product propylene (Scheme 3, 5a) were detected (Figs. S1, S2). In addition, when **1ab** and **1ac** were employed for the deally-

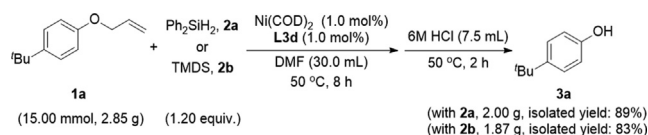
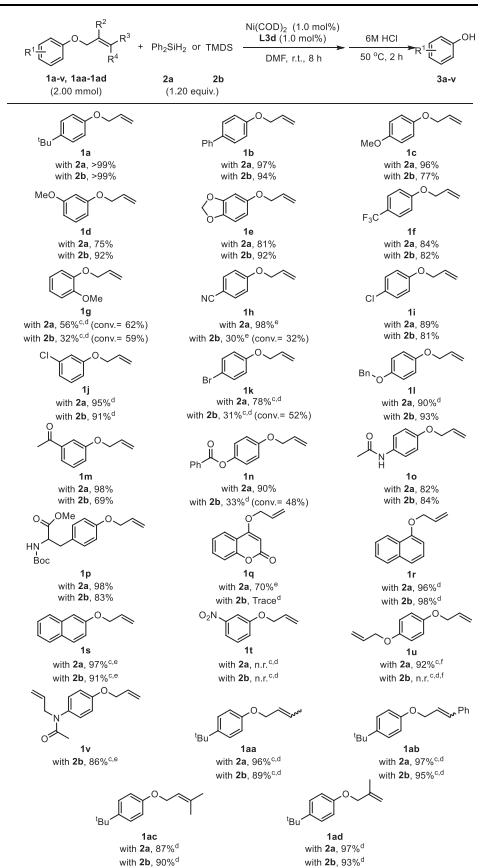
**Scheme 2.** Gram-scale reactions.

Table 2
Substrate scope.^{a,b}

^aReagents and conditions: aryl allyl ether (**1**, 2.00 mmol), **2a** or **2b** (2.40 mmol), Ni(COD)₂ (1.0 mol%), **L3d** (1.0 mol%), DMF (5.0 mL) under a N₂ atmosphere, room temperature, 8 h.

Then, 6 M HCl (1.0 mL), 50 °C, 2 h.

^bIsolated yields of corresponding phenol product **3**.

^cNi(COD)₂ (2.0 mol%) and **L3d** (2.0 mol%).

^d80 °C.

^e50 °C.

^f**2a** or **2b** (4.80 mmol).

lation, the corresponding olefin products (*E*)-prop-1-en-1-ylbenzene (**5ab**) and 2-methylbut-2-ene (**5ac**) were also successfully isolated or detected (Figs. S3–S5), which could also help to exemplify the catalytic cycle. Therefore, the nickel-catalyzed deallylation underwent the cleavage of C–O bond of allyl ethers to form η^3 -allylnickel intermediate, followed by the reaction with hydrosilanes. The plausible reaction mechanism was shown as Scheme 3.

Initially, Ni(0) bipyridine compound undergoes oxidative addition with the substrate **1** to give η^3 -allylnickel species **I**. Then **I** is attacked by Ph₂SiH₂ to afford the nickel hydride **III** and the silyl aryl ether intermediate **II** or **II'**. The intermediate **II** or **II'** can be hydrolyzed under mild acid conditions to yield the desired deallylation product **3**. Facile reductive elimination of **III** furnishes propylene (**5a**) and regenerates Ni(0) for the next catalytic cycle.

Conclusion

In summary, we developed a nickel-catalyzed deallylation method of aryl allyl ethers. By using commercially available Ni(COD)₂ as catalyst precursor, simple substituted bipyridine as ligand and air-stable and easily available hydrosilanes, the desired phenol products were obtained in excellent yields and selectivity under mild reaction conditions. The method is compatible with a variety of functional groups and is also effective for the removal of substituted allyl protecting groups. Mechanism studies indicate it undergoes the η^3 -allylnickel intermediate pathway.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

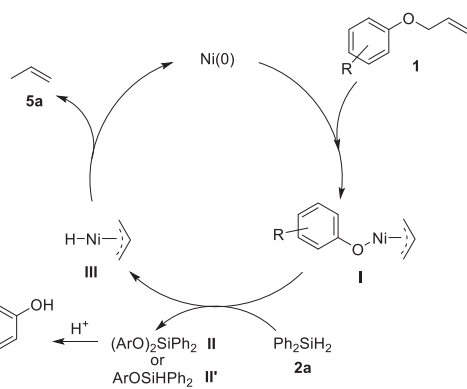
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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.tetlet.2021.153341>.

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